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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,094	10/22/2003	John H. Griffin	P-144-US2	4781

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EXAMINER	
COPPINS, JANET L	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 02/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/691,094	GRIFFIN ET AL.	
	Examiner	Art Unit	
	Janet L. Coppins	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 4/21/04.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 22-33 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 22-33 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 22-33 pending in the instant application.

Preliminary Amendment

1. Receipt is acknowledged of Applicants' Preliminary Amendment, filed October 22, 2003. Accordingly, claims 1-21 have been cancelled, claim 22 has been amended, and new claims 23-33 have been added.

Information Disclosure Statements

2. Receipt is acknowledged of Applicants' Informational Disclosure Statement (IDS), filed January 9, 2004, which has been considered by the Examiner. Please refer to Applicants' copy of the PTO-1449 form submitted herewith.

Telephone Interview

3. In a conversation with Applicants' attorney, Robert P. Saxon, Reg. No. 43,087, on January 14, 2005, the Examiner proposed canceling claims 25, 26, 31, and 32, and combining the diseases of claim 28 into claim 22 as well as the disease of claim 33 into claim 28. Applicants did not accept the proposal and preferred to pursue the claims as currently presented.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 22-33 rejected under 35 U.S.C. 112, first paragraph, as not being fully enabled. While the various proliferative diseases/disorders may be listed on page 9 of the specification, the claims are not enabled for *all* proliferative diseases or *all* cancers, since

there is no indication as to the full range of proliferative diseases or cancers that could be treated using the instant claimed process.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention;
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, the claims are directed to many diseases and conditions that are not enabled in the specification, including those broadly recited in claims 22-25 and 28-31.

The nature of the invention

The nature of the invention is of methods of treating many different diseases or conditions that involve the tyrosine kinase receptor, comprising administering the instant claimed compound to a patient in need thereof.

The state of the prior art and the predictability or lack thereof in the art

It is well recognized in the medical art that treatment of diseases or symptoms are not analogous terms. Furthermore, the diseases listed in the description on page 9 of the specification are not the same but include different cancers as well as restenosis. The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of

these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. Also, in the absence of a showing of correlation between all the diseases claimed as capable of being treated by the compound of claim 1 and the response of the tyrosine kinase receptor, one of skill in the art is unable to fully predict possible results from the administration of the compound of claim 1.

The amount of direction or guidance present

The specification has enabled only the compounds according to claim 1 that selectively inhibit a tyrosine kinase receptor-mediated response. Furthermore, treatment of the claimed broad range of diseases are normally disease or symptom oriented, thus are highly individualized, i.e. treating each and every disease encompassed by the claimed "proliferative diseases" would not employ the same methods. The efficacy of an individual compound against a specific disease or symptom needs to be specifically and individually supported by factual evidence. Such evidence has not been described or supported by the specification.

The presence or absence of working examples

The data provided in the disclosure is insufficient evidence for methods of treating all claimed proliferative diseases. In fact, the only disclosure in the specification at all is found on pages 25-28 wherein an *in vitro* binding assay is described, wherein displacement of a radiolabeled test ligand from the tyrosine kinase receptor subtype is measured. Applicants have provided evidence that the compounds are effective for inhibiting receptor tyrosine kinases within AML cell lines, however "the selection of the examples...used as the disclosure to support a claim must be adequately representative of

the area covered by it," please see *In re Cavallito et al.* (CCPA 1970) 429 F2d 452, 166 USPQ 552. Therefore the specification is enabled for certain proliferative diseases limited to the following specific cancers: acute myeloid leukemia, small cell lung cancer, prostate cancer, gastrointestinal cancer, breast cancer and brain cancer, as well as restenosis; however the instant specification is lacking significant data to accommodate as many cancers as the claims are alleging by reciting the broad terms "cancer" or "growth of a solid tumor."

The breadth of the claims

Applicants are claiming methods of treating a broad number of diseases or conditions. The argument that the diseases claimed by the Applicants are all treated by inhibiting the tyrosine kinase receptor is insufficient support that the claimed compounds have specific efficacy in current available form for treating all of the diseases and cancers encompassed by the broadly recited "proliferative diseases" or "cancer."

The quantity of experimentation needed

The quantity of experimentation needed is undue. One of ordinary skill in the art without direction, would be unable to treat each and every disease/condition encompassed by claims 22-26 and 28-32, using the instant claimed compounds. One of skill in the art would need to determine what proliferative diseases would be benefited by the inhibiting the tyrosine kinase receptor and would furthermore then have to determine whether the claimed compounds would provide treatment of all of the diseases and conditions by said activity.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the

pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the claim I for the treatment of all proliferative diseases in claims 22-25, and 28-31 as well as all cancers of claims 26 and 32. As a result, necessitating one of skill to perform an exhaustive search for which claimed diseases can be treated by the compound of claim I in order to practice the claimed invention.

Regarding claims 26, 27, 32 and 33, due to the unpredictable nature of cancer and the fact that over 3,000 different cancers exist, the various types of cancers have different causative agents, involve different cellular mechanisms, and differ in treatment protocol, thus no single compound exists presently that is known to treat *all* cancers as a blanket therapeutic. Furthermore, the Merck® manual currently has many cancer treating agents (over 12,000 compounds), yet they are only known to treat one cancer each. The Examiner suggests narrowing the scope of the diseases and cancers claimed in claims 22-26 and 28-32, as well as specifying which tumor in claims 27 and 33.

6. Claims 22 and 28 also rejected under 35 U.S.C. 112, first paragraph, as being reach-through claims. These claims are directed to a method of treating diseases wherein the tyrosine kinase receptor is implicated, yet these claims do not meet the requirements for "how to use" under 35 U.S.C. 112, first paragraph, and 35 U.S.C. 101, as stated below. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility, or a well established utility for the reasons set forth below,

one skilled in the art clearly would not know how to use the claimed invention. The claims are directed to a method of treating a condition responsive to a tyrosine kinase inhibitor, yet the claim fails to present a tangible use. The Examiner suggests claiming the possible diseases and conditions that are treated, rather than claiming the mechanism, which is speculative.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Regarding claims 22-24 and 28-30, applicant states that the invention may be used to treat diseases that can be influenced positively by inhibiting tyrosine kinase but does not provide examples as such. Receptor tyrosine kinase inhibitors are suitable for treating certain proliferative diseases, and are desirable in the treatment of diseases found on page 9 of the specification, such as restenosis, breast cancer, prostate cancer, etc. Without further clarification, however, it is unclear what diseases the Applicants are intending to encompass.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 22 and 28 rejected under 35 U.S.C. 101 as being reach-through claims, because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The claimed method of treating a condition responsive to a tyrosine kinase inhibitor does not comply with the utility requirement since there is no disclosed pharmaceutical use, i.e. a method of treating a disease wherein

inhibiting tyrosine kinase receptors has a beneficial effect is not equivalent to a positive recitation of how to use the product for the treatment of a particular disease of real world relevance. The Examiner suggests incorporating some of the specific diseases that Applicants are enabled for treating in the specification.

Conclusion

11. In conclusion, claims 22-33 are pending. Claims 22-33 stand rejected. Claims 28 and 33 (excluding "growth of a solid tumor") would be allowable if they were combined with claims 22 and 28, respectively, such that the claims read, "A method of treating a condition responsive to a tyrosine kinase inhibitor, wherein the condition is selected from the group consisting of acute myeloid leukemia, small cell lung cancer, prostate cancer, gastrointestinal cancer, breast cancer, brain cancer, and restenosis, the method comprising administering to a patient in need of treatment...".

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 571.273.8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Coppins
January 26, 2005

for Kamal Saeed
Joseph K. McKane
SPE, Art Unit 1626